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Resident Poster Abstract

Name of Residency Site: San Antonio Combined Military Medical Center, San Antonio, TX

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Submission Category: Emergency Preparedness

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Submission Type: Research-in-Progress-Report

TITLE (limit 25 words): Pyridostigmine bromide 30mg stability in extended storage conditions

PURPOSE (limit 100 words): Pyridostigmine bromide 30mg is approved by the Federal Drug Administration (FDA) as a pre-treatment of nerve gas exposure. The package insert specifies pyridostigmine needs to be refrigerated while stored and discarded three months after removal from the fridge and dispensing. The objective of this study is to determine the stability of pyridostigmine under extended storage conditions.

METHOD (limit 200 words): The study will be submitted to the Institutional Review Board as a non-human study. Two hundred and ten pyridostigmine tablets from the same lot will be stored under controlled temperature and humidity. The tablets will be tested at 0, 3, 4, 5, and 6 months after removal from refrigerator when stored at both ideal and manipulated storage conditions. The ideal storage conditions will be defined as controlled room temperature as specified by the United States Pharmacopeia (USP) <659>. The real-life storage conditions will be determined using the International Commission for Harmonization's (ICH) Quality Guidance definitions of storage conditions required for stability testing to obtain new drug approval in different climate zones in the world. At each testing interval, tablet samples will be removed from the manufacturer's packaging and analyzed using high-performance liquid chromatography (HPLC) and mass spectrometry to determine the content of the drug substance in the tablets (assay) and to assess the degradation by-products. Each measurement will be performed in triplicate. The ICH definition for significant change (a change from the initial content of 5% or more as detected by assay) will be used to determine pyridostigmine stability at the end of each testing periods.

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Pyridostigmine Bromide 30mg Stability in Extended Storage Conditions

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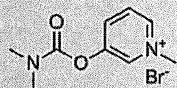
Brooke Army Medical Center, Joint Base San Antonio, San Antonio, TX



BACKGROUND

Pyridostigmine bromide 30mg is indicated for military medical use as a pretreatment for Soman gas when used in conjunction with injections of atropine and pralidoxime, and protective garments.

Pyridostigmine bromide ($C_9H_{13}BrN_2O_2$) is a carbamate-based acetylcholinesterase (AChE) inhibitor that prevents the hydrolysis of acetylcholine (ACh) in the peripheral nervous system.



AChE inhibition results in ACh accumulation at cholinergic synapses which facilitates impulse transmission across the neuromuscular junction. Unlike organophosphates, carbamates are considered reversible AChE inhibitors because they can be split from AChE by spontaneous hydrolysis. Consequently, they exhibit a protective effect when used before irreversibly-binding organophosphates, like nerve gases.¹

In 2003 the Federal Drug Administration (FDA) approved pyridostigmine bromide 30mg tablets to increase survival after exposure to nerve gas.² The package insert specifies the tablets must be stored refrigerated between 2 and 8°C prior to dispensing and instructs military personnel to discard the contents of the individual packages three months after issue.³

To date, studies have not been conducted to determine the stability of pyridostigmine bromide 30mg tablets beyond the three months in temperatures higher than 2-8°C.

OBJECTIVE

The purpose of this study is to determine the stability of pyridostigmine bromide 30mg tablets up to six months after removal from refrigeration in varying temperature and humidity storage conditions.

METHODS

- Stability is defined as the retention of at least 95% of the labeled concentration.
- Pyridostigmine bromide 30mg tablets will be assayed in triplicate at five time points and four temperature and humidity conditions (0, 3, 4, 5, and 6 months).
- Storage definitions:
 - Ideal storage conditions are defined as controlled room temperature per the United States Pharmacopeia <659>, Packaging and Storage Requirements.⁴
 - Real-life storage conditions are defined based on the International Council for Harmonisation's (ICH) Quality Guidance, which the FDA recognizes as the governing document for drug stability testing requirements and procedures in the United States.
- To guide the member states on long-term drug stability testing conditions, the ICH uses the World Health Organization's definition of climatic zones.⁵ Based on the guidance, four storage conditions were identified as optimal to simulate four climatic zones and one accelerated study storage condition (Table 1).
- Samples will be analyzed in triplicate using two methods: high-performance liquid chromatography to determine the content of the drug substance in the tablets (assay) and mass spectrometry to assess degradation by-products.

Pyridostigmine bromide 30mg unit-of-use package

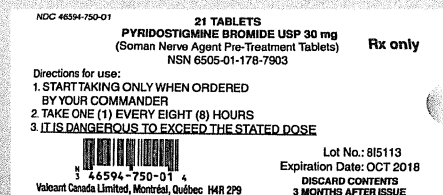


Table 1. Data Collection Form [mean (SD) percentage of labeled amount]

Testing interval	Storage Conditions							
	25±2°C 60±5% RH		30±2°C 65±5% RH		30±2°C 35±5% RH		40±2°C 75±5% RH	
	HPLC	MS	HPLC	MS	HPLC	MS	HPLC	MS
0 months								
3 months								
4 months								
5 months								
6 months								

RH: relative humidity

HPLC: high-performance liquid chromatography

MS: mass spectrometry

RESULTS

Pending. Storage conditions testing is scheduled for 1 Nov 2017 - 30 Apr 2018. To avoid a potential variability in instrument calibration and testing procedure all samples will be analyzed at the conclusion of the trial.

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DISCLOSURES

Financial: Joanna Heskett and Irene W. Lo declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this poster, including grants, employment, gifts, stock holdings, and honoraria.

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